Pancreatic islet and stellate cells are the main sources of endocrine gland-derived vascular endothelial growth factor/prokineticin-1 in pancreatic cancer.

AIMS: Endocrine gland-derived vascular endothelial growth factor (EG-VEGF)/prokinetics have been identified as tissue-specific angiogenic factors. This study investigates the expression and localization of EG-VEGF and its receptors in pancreatic tissues and pancreatic stellate cells (PSCs). METHODS: mRNA levels of EG-VEGF/prokineticin 1 (PK1), prokineticin 2 (PK2) and their receptors 1 (PKR1) and 2 (PKR2) were measured in pancreatic tissues, pancreatic cancer cell lines and PSCs by quantitative reverse-transcriptase polymerase chain reaction (QRT-PCR). Protein expression of PK1, PKR1 and PKR2 was assessed in pancreatic tissues by immunohistochemistry. Growth factor-induced secretion of EG-VEGF was measured by ELISA. RESULTS: QRT-PCR analysis in bulk tissues of normal pancreas, chronic pancreatitis, chronic pancreatitis and pancreatic ductal adenocarcinoma showed no significant difference of PK1 mRNA levels, whereas PK2 mRNA was barely detectable. High PK1 mRNA levels were observed only in cultured PSCs and microdissected islet cells, but not in cancer cells, and PK1 protein was localized mainly in islets and cancer-associated stromal cells. PKR1 and PKR2 proteins were present in endothelial cells of small blood vessels. TGF-beta(1) and PDGF-BB specifically stimulated PK1
secretion in PSCs. CONCLUSIONS: Islet and/or PSC-derived PK1 might act through its receptors on endothelial cells to increase angiogenesis in pancreatic diseases.